PATENT
3657-1037

IN THE U.S. PATENT AND TRADEMARK OFFICE

In re application of

Geir CHRISTENSEN et al. Conf. 6193

Application No. 10/585,077 Group 1633

Filed September 7, 2006 Examiner Anne Marie Sabrina Wehbe

NON-HUMAN MAMMAL COMPRISING A MODIFIED SERCA2 GENE AND METHODS, CELLS, GENES, AND VECTORS THEREOF

DECLARATION UNDER RULE 132

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

CONSIDERED: /AW/ (06/29/2011)

Sir:

I, Dr. Frank WUYTACK, hereby declare as follows:

I am an expert in the field of molecular and cell biology and in the subject of ATPase enzymes. I am Professor in the Department of Molecular Cell Biology, Laboratory of Ca^{2+}-transport ATPases, K.U. Leuven, Campus Gasthuisberg O&N1, LEUVEN, Belgium.

I have read the Office Action mailed December 9, 2010, and I am familiar with the present application.

The Office Action does not appear to fully appreciate the teachings of the cited references.

PERIASAMY et al. investigated the function of the SERCA2 gene in heart disease and utilized a SERCA2 knockout mouse system. PERIASAMY observed that mice with heterozygous mutation

in SERCA2, while not exhibiting overt heart disease, exhibited some changes in Ca^{2+} signaling and in blood pressure levels. Further, PERIASAMY highlighted that homozygous SERCA2 mutants are embryonic lethal and do not survive. Thus, PERIASAMY found it necessary to perform the studies on heterozygotes.

SOHAL et al. teaches that the embryonic lethality can be circumvented by the use of an inducible tissue specific Cre-Lox system. By using this system, the gene under study typically remains intact at the embryonic stage but can be disrupted at a later stage, thereby avoiding any embryonic lethality. Therefore, when the gene under study is critical for life at all stages (i.e., at both the embryonic stage and at the adult stage), the SOHAL system can be used to circumvent embryonic lethality and allows one to assess adult lethality.

SERCA2 (Atp2A2) is a gene which as of December 30, 2003 (the priority date of the present application) was considered to be critical for life, both at the embryonic stage and at the adult stage. If the system disclosed in SOHAL was to be used then it would be highly probable that a mouse lacking a functional SERCA2 ATPase at the adult stage would not survive for long, and in particular, not survive for more than about one week. This is in agreement with the conclusion reached by PERIASAMY who found it necessary to perform there studies with heterozygotes.

What was unexpected, however, and hence of interest, was that the mice survived the induced removal of SERCA2 at the

adult stage for up to 7 or 8 weeks, i.e. much longer than one would have predicted. Accordingly, one of ordinary skill in the art as of the priority date of the present application would have no reasonable expectation of success (i.e., homozygous SERCA2 mutants which survive more than 5 weeks) by combining the knowledge of PERIASAMY with that of SOHAL.

I have no interest in the present patent application.

I further declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under §1001 of Title 18 of the United States code and that such willful false statements may jeopardize the validity of the application or any patent issuing thereon.

Dr. Frank WOYTACK

Date March 25 2011